REMARKS

The present paper is filed in response to a non-final office action dated June 23, 2011. A response is due on December 23, 2011 by virtue of the attached petition and fee for a three-month extension of time to respond.

Status of Claims

Claims 97, 157-175, 177-182 and 184-188 are pending and under examination and have been rejected in the following rejections:

- Claims 181-182 and 186 under 102(b) over US Patent 4,994,373
- Claims 181-182 and 186 under 102(e) over US Patent 5,556,748
- Claims 181-182 and 186 under 102(e) over US Patent 5,494,810
- Claims 181-182 and 184-188 under 103(a) over US Patent 5,494,810
- Claims 97, 157-175, 177-182, 184, 186-187 under 103(a) over Southern in view of Kauver and/or Wang
- Claims 97, 157-175 and 177-189 under 103(a) over Drmanac in view of Kauver and/or Wang

Applicants respectfully traverse the rejections and request reconsideration of the rejections in view of the instant response and the comments previously of record.

Support for Claim Amendments

The amendment to claims 97 and 166 to include the term "to permit parallel execution of reactions in said microchips" is supported in the specification at page 44, lines 7-16 (page numbering according to original PCT specification) which states:

> "Two basic problems have to be solved. Manipulation with small (2-3 mm) chips, and **parallel execution of thousands of the reactions**. The solution of the invention is to keep the chips and the probes in the corresponding arrays. In one example, chips containing 250,000 9-mers are synthesized on a silicon wafer in the form of 8x8 mM plates (15 μM/oligonucleotide, Pease et al., 1994) arrayed in 8x12 format (96 chips) with a 1 mM groove in between. Probes are added either by multichannel pipet or pin array, one probe on one chip."

Rejections under 102(b) in view of US Patent 4,994,373, and 102(e) in view of US Patent 5,556,748, and 102(e) in view of US Patent 5,494,810

The rejection of Claims 181-182 and 186 under 102(b) in view of US Patent 4,994,373, and 102(e) in view of US Patent 5,556,748, and 102(e) in view of US Patent 5,494,810 are overcome by the amendment of claim 181 to incorporate the features of claim 184 (which is now cancelled), the amendment of claim 185 to be written in independent format, the amendment of claim 186 to incorporate the features of claim 187 (which is now cancelled), and the amendment of claim 188 to be written in independent format.

Applicants respectfully request withdrawal of the rejection of claims 181-182 and 186 and reconsideration of the claims for allowance.

Rejections under 103(a) in view of US Patent 5,494,810

Claims 181-182 and 184-188 were rejected under 103(a) in view of U.S. Patent 5,494,810. Applicants respectfully traverse this rejection. These claims are directed to an apparatus comprising a solid support comprising a plurality of sections, each section comprising an array of oligonucleotides attached to the support. The sections are separated from each other by physical barriers or hydrophobic strips.

US Patent 5,494,810 teaches an array of **individual wells** comprising immobilized analytes. At best this can be seen as a single array, not a plurality of arrays. In US Patent 5,494,810 Barany shows biotinylated oligonucleotides immobilized in the wells of a microtiter plate via streptavidin coating the wells. Even if each well has multiple immobilized oligonucleotides, the immobilized oligonucleotides in each well are not in an orderly arrangement in the wells so as to constitute an array. The word "array" or "microarray" is well understood by the skilled person. For example, the American Heritage Science Dictionary (© 2005 Houghton Mifflin Company) defines "DNA microarray" to mean "a small solid support, usually a membrane or glass slide, on which sequences of DNA are fixed in an orderly arrangement." The skilled person would not understand the multiple oligonucleotides or other analytes that are immobilized in wells or depressions to be in such an orderly arrangement so as to constitute an array. Barany does not teach a plurality of sections, each section comprising an array of oligonucleotides attached to the support, as required by claims 181, 182 and 186. The modifications suggested by the Examiner do not address this deficiency: even with such modifications, only one array is taught by Barany, not a plurality of arrays with the

recited features. Barany fails to meet the requirement for obviousness that requires each element of the claim to be present in the cited art.

Applicants respectfully request reconsideration of the rejection in view of the amendments to the claims and lack of disclosure in US Patent 5,494,810.

Rejections under 103(a) over Southern in view of Kauver and/or Wang

The Examiner maintains the rejection of claims 97, 157-175 177-182, 184 and 186-187 over Southern in view of Kauver or Wang. Applicants respectfully traverse the rejection.

The Examiner provides a detailed breakdown of the features of certain independent claims that are found in the secondary references. The Examiner does note that the asserted utility is noted but the claims are not limited to that intended use as asserted. In order to address this issue, Applicants have amended the claims to include the phrase "to permit parallel execution of reactions in said microchips" Applicants submit this amendment adds the asserted utility to the claims. Applicants submit that the analysis in the office action still fails to take into account that Southern does not teach any mechanism for keeping separated the arrays and probes and that neither Kauver nor Wang provide this teaching. In the absence of such separation Southern cannot execute parallel reactions on the device disclosed therein and addition of Kauver or Wang to Southern fails to remedy this deficit.

Kauver's discussion of measuring methyl mannose and its binding to Conconavalin A is irrelevant to a discussion of the present invention which is used to

measure different oligonucleotides which have different structures from each other. For Kauver's measurement of a single molecule there is no need to separate out the methyl mannose into separate arrays for separate reactions because all of the methyl mannose will have the same structure. Figure 3 of Southern merely shows an arrangement of 4 arrays of oligonucleotides but each array is identical in terms of the oligonucleotides that are attached to each array so that replicate measurements of the same reaction are taken on the four arrays. There is no barrier or other manner of containing the reaction mixtures so that different hybridization reactions using different labeled probes can on the separate individual unit arrays of Southern. The arrays of Southern simply lack separation of the unit arrays which permit separate and parallel execution of sequencing reactions and hence any attempt to perform such multiple reactions on the Southern array would not be effective because the reaction mixture from one array would bleed into another and obscure the results obtained.

The skilled person would not be motivated to combine Kauver with Southern because Kauver is directed at increasing the sensitivity of binding of a single sugar moiety of known structure to a lectin. This has nothing to do with sequencing oligonucleotides. There is nothing in Kauver that suggests that a platform used to detect sugars would be useful for detecting oligonucleotides. The two endeavors (detection of a sugar using conconavalin A versus determining the structure of an oligonucleotide by hybridizing it to a complementary oligonucleotide probe) are two different fields of endeavor and there is no teaching in Kauver that the methods used in the detection of a sugar are applicable to techniques of sequencing. Southern relates to concerned with sequencing (i.e., determining the structure of) a target nucleic acid

sequence of unknown structure by determining which known counterpart nucleic acid the unknown target sequence binds to. The binding only happens where there is complementarity between the target sequence and the oligonucleotide probe. These are two different technical fields of endeavor and the mere fact that Kauver asserts that it has an interest in region-specific signal detection for "convenience and simplicity of interpreting results" does not overcome the fact that Kauver already knows the identity of the thing being detected and the method of Kauver provides no structural information about the mannose detected. This argument while relating to the use of the Southern arrays as compared to Kauver is central to the differences in format of the Southern array and Kauver technique and why it is not necessarily predictable that a teaching fro Kauver should be imported into the teaching of Southern without some nexus between the two.

Wang again is simply related to creating a matrix with a barrier pad in it that is impregnated with hydrophobic material. There is nothing in Wang that shows why doing so would lead to a better hybridization array of Southern. Southern adequately achieved sequencing of a small target nucleic acid in a particular type of sequencing by hybridization reaction. Use of the four arrays was, as noted by the examiner, to increase region specific signal detection using the same reaction conditions for all four arrays. Southern was not concerned with needing to perform multiple hybridization reactions using different sets of probes on the same array and hence Southern did not require separation of the arrays. Indeed, separating the arrays of Southern would have created an impediment or delay in the assay in that same reaction mixture would have to be supplied in four steps to the four separate arrays.

The combination of Drmanac with the remaining references also does not render obvious the presently claimed invention. The Drmanac reference relates to sequencing a target nucleic acid wherein the target nucleic acid is immobilized on the substrate. The detection in Drmanac is achieved by adding labeled probes to the immobilized target. The fact that the probes are not immobilized in the Drmanac reference means that the need for separation of the different areas of the substrate is not necessary because the different areas of the substrate are all coated **with the same molecule of one structure**, i.e., the target that is to be sequenced. Given that there is no need to separate the different areas of the target bound substrate there would be no reason for the skilled person to modify the Drmanac reference with teachings that show hydrophobic or other separation barriers.

In view of the amendment to the claims and the above remarks Applicants believe the rejection should be withdrawn and respectfully request reconsideration of the claims for allowance.

The Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

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